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The Failure of Radiophosphorus to Identify Malignant Solitary Thyroid Nodules[1]

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The management of the clinically solitary thyroid nodule remains one of the more difficult problems faced by endocrinologists and thyroid surgeons (1). Although the majority of nodules are benign, a few of them are malignant. There are no clinical features which will distinguish the malignant nodules from the benign, unless extracapsular invasion, spread to cervical nodes, or distant metastasis has occurred (2). In the early stages, these malignant lesions, although usually firm or hard, may be soft, rubbery, smooth, or rounded and mobile. Most literary reports give an incidence of malignancy in solitary thyroid nodules of about ten per cent (3).

The use of radioiodine has been of some help in distinguishing malignancy (4,5), for iodine concentrates less efficiently in thyroid carcinoma cells than in normal cells. Therefore, malignant lesions appear as nonfunctioning areas, *i.e. cold* nodules, or as poorly functioning areas, *i.e. cool* nodules. Nevertheless, many *cool* and *cold* nodules prove to be benign.

Bauer (6) in 1959, and Ackerman (7,8), in 1960, reported a higher uptake of radiophosphorus by malignant nodules than by benign nodules. This increased concentration of radiophosphorus could result from its incorporation into the nuclei of multiplying neoplastic cells, for ^{32}P would then persist in the lesion until the cells containing it were dead. Thus, it appeared reasonable to study solitary thyroid nodules with both ^{32}P and ^{131}I in the hope of providing an accurate diagnosis as far as malignancy is concerned.

METHODS

In the past two years, most of the patients for radioiodine studies referred to the Isotope Department of The Princess Margaret Hospital and were investigated by using both ^{32}P and ^{131}I, if they were found to have a clinically solitary nodule. All who agreed to the additional ^{32}P study were included in this series. Seventy patients were studied.

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PHOSPHORUS-32

Intravenously, 200μC of ^{32}P were given. Twenty-four hours later, readings were made over the nodule and over normal thyroid tissue, using an end-window Geiger-Mueller tube, which is efficient in counting the β-emission originating 6-7 mm or less below the skin surface. The ^{32}P uptake in the nodule was expressed as the ratio of cpm over nodule to cpm over normal thyroid tissue. As suggested by Ackerman, a significant increase was taken to be 1.25 or greater.

Initially, readings were made at two hours, and again at 24 hours. Because the ratio was the same or higher at 24 hours, the two hour readings were omitted in the later studies.

IODINE-131

After completing the ^{32}P readings, the patient was given 20-50 μC of ^{131}I orally, and 24 hours later a thyroid uptake and scan were done. The outline of the nodule was recorded on the scan at the time that the scan was being carried out. The nodule was then classified as *hot, warm, cool* or *cold,* depending upon the demonstration of increased, comparable, decreased, or absent radioiodine concentration, compared to the normal parts of the gland.

RESULTS

Although 70 patients were studied, only 25 have a definitive diagnosis. Twenty-three underwent surgery, and the nodule completely disappeared in the other two patients.

There were six patients with carcinoma, but only one had an elevated ^{32}P uptake, 1.32. In the other five patients, the uptake ranged from 0.85 to 1.06. Three were *cold* to radioiodine, and three were *cool.* Thus, all six demonstrated decreased function.

The six patients with benign adenomas had two nodules that were *hot,* with respect to ^{32}P, 1.27 and 1.54. The latter contained areas of microscopic calcification, which was probably the cause of the very high ^{32}P uptake. The radioiodine scans revealed two *hot* nodules, one *cool* nodule, and three *cold* nodules.

None of the 10 patients with adenomatous goiter had an increased ^{32}P uptake; most were in the 0.90 to 1.10 range, although the reading in one patient was 1.23. With radioiodine, two were *hot,* two were *warm,* two were *cool,* and three were *cold.* The uptake in the remaining patient was too low to judge the function of the nodule.

The one patient with a thyroglossal duct cyst had a ^{32}P uptake of 1.16 and was *hot* with respect to ^{131}I.

One patient had a nodule which was *cool* to both ^{32}P and ^{131}I; it disappeared completely after six months of thyroxine therapy. Another patient had a nodule which had a ^{32}P uptake of 1.28 and was *cool* to radioiodine. The nodule had completely disappeared when the patient was admitted for surgery six weeks later. She had received no therapy in the interval.

DISCUSSION

The technical problem of accurately measuring β-emission from tissues beneath the skin is due to the short tissue distance which β particles can traverse. Therefore, in performing these measurements, it is essential that some pressure be used so that as little tissue as possible is present between the nodule and the end of the G-M tube. It is probable that the technique was satisfactory in at least some patients, for four of the 25 nodules did have a significant increase in concentration of ^{32}P. The one malignant nodule with an increased ^{32}P uptake was very small, 3 × 1.5 cm. The only large malignant mass, 8 cm in diameter, had an uptake of 1.06, yet the tissues between it and the skin must have been thinned considerable.

From these results, it would appear that radiophosphorus concentration is not useful in establishing the diagnosis of malignancy, for three of the four nodules with an increased uptake were benign. Even more distressing is the inability of this test to exclude malignancy, for five of the six malignant nodules did not have an increase in ^{32}P uptake.

All six malignant nodules also demonstrated a decreased function with respect to radioiodine, whereas, seven of the 19 benign lesions concentrated radioiodine to a significant extent.

TABLE I

	Clinically Solitary Thyroid Nodules				
	^{32}P *cpm, nodule/cpm, gland*		^{131}I		
	< 1.25	*> 1.25*	*Hot or Warm*	*Cool*	*Cold*
Carcinoma	5	1 (1.32)	—	3	3
Adenoma	4	(1.27) 2 (1.54)	2	1	3
Nodular Goiter	10	—	4	2	3
Thyroglossal Duct Cyst	1	—	1	—	—
Disappeared	1	1 (1.28)	1	1	—

SUMMARY

Only one of six patients with malignant thyroid nodules showed an increased concentration of radiophosphorus. Two of the six benign adenomas, and one other benign nodule also concentrated radiophosphorus significantly. Thus, the concentration of ^{32}P appears to be of little value in the exclusion or establishment of malignancy in clinically solitary thyroid nodules. As reported, radioiodine scans are of some value in this respect.

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CORRECTION NOTICE

It was brought to our attention by Edward M. Smith, Sc.D., author of the article, "Internal Dose Calculations for Tc-99m", that there were several mistakes in his article which appeared in the April 1965, issue of the journal. These occur on page 247 and page 248.

On page 247, TABLE VIII, under the heading *From γ Type Radiation,* 0.8 should read 13. Therefore, the first *Total* should read 17 instead of 5. On page 248, TABLE X, 1.1 under the heading *Liver* should read 1.6.